510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE AND INSTRUMENT TEMPLATE

A. 510(k) Number:
K031739

B. Analyte:
Troponin I

C. Type of Test:
Electrochemical two site ELISA

D. Applicant:
i-STAT Corporation

E. Proprietary and Established Names:
i-STAT® cTnI Test

F. Regulatory Information:

1. Regulation section:
   21 CFR §862.1215

2. Classification:
   Class II

3. Product Code:
   MMI

4. Panel:
   Chemistry (75)

G. Intended Use:

1. Intended use(s):
   The i-STAT® cTnI Test is an *in vitro* diagnostic test for the quantitative measurement of cardiac troponin I in heparinized whole blood or plasma samples. Cardiac troponin I measurements can be used as an aid in the diagnosis and treatment of myocardial infarction and in the risk stratification of patients with acute coronary syndromes with respect to their relative risk of mortality.
   The cartridge is to be used with the i-STAT 1 Analyzer, but not the i-STAT Portable Clinical Analyzer or the Philips Medical Systems (formerly Agilent Technologies) Blood Analysis Module (BAM). As part of the i-STAT

System, the cTnI test is to be used by trained health care professionals in accordance with a facility's polices and procedures.

2. Indication(s) for use:
   The i-STAT Cardiac Troponin I (cTnI) test is an in vitro diagnostic test for the quantitative measurement of cardiac troponin I in heparinized whole blood or plasma. Measurements of cardiac Troponin I are used in the diagnosis and treatment of myocardial infarction and as an aid in the risk stratification of patients with acute coronary syndromes with respect to their relative risk of mortality.

3. Special condition for use statement(s):

4. Special instrument Requirements:
   i-STAT 1 Analyzer

H. Device Description

The i-STAT cTnI is contained in a single cartridge. In use, the user scans a barcode and then places approximately 16 microliters of fresh whole blood in the cartridge. The cartridge is inserted into the thermally controlled i-STAT 1 Analyzer, and all analytical steps are performed automatically. Patient and user information may be entered into the analyzer via a keypad during the automated analysis cycle. The cTnI test cartridge is assembled from plastic components that provide the conduits for fluid handling and house the sensor chips and heating elements necessary for temperature control and signal measurement.

Upon insertion of the cartridge into the analyzer, it performs several quality checks. The sample and enzyme-linked antibody conjugate are incubated for a predetermined period of time under temperature control. The sample is discarded and the substrate/wash solution is brought over the alkaline phosphatase captured on the cTnI sensor. The enzyme cleaves the substrate giving rise to an amperometric signal which the analyzer measures. The result is displayed and stored in memory for possible transfer via infra red to a printer or to electronic databases.

I. Substantial Equivalence Information:

1. Predicate device name(s):
   Dade Behring Stratus® CS Cardiac Troponin I TestPak

2. Predicate K number(s):
   K981098

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Assay Methodology	Two Site ELISA	Two Site ELISA
Capture antibodies	Monoclonal	Monoclonal
Enzyme label	Alkaline Phosphatase	Alkaline Phosphatase
Differences		
Item	**Device**	**Predicate**
Enzyme detection	Electrochemical	Fluorescent
Sample type	Whole blood or Plasma	Plasma
Enzyme label antibody	Polyclonal	Monoclonal

J. Standard/Guidance Document Referenced (if applicable):

FDA's *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices.*

NCCLS guideline EP9-A2: *Method Comparison and Bias Estimation Using Patient Samples*.

Conforms to EN61326 EMC.

K. Test Principle:

Two Site Elisa. The analyte, cardiac Troponin I is captured by a probe impregnated with a monoclonal anti-cTnI antibody. The sample is discarded. The probe is treated with a second reagent composed of anti-cTnI polyclonal antibodies which are tagged with Alkaline Phosphatase. After washing, the sandwich complex is treated with a substrate which upon being cleaved by the captured alkaline phosphatase produces and electronic signal which is read by the i-STAT analyzer.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Three levels of plasma controls were tested as duplicates 20 times over a period of 37 days in four different locations (in-house and three clinical sites) using three different lots of i-STAT cTnI cartridges with 25 different i-STAT analyzers.

Site	Control Level	Mean	Within-Lot %CV	Lot-to-Lot %CV	Vial-to-Vial %CV	Total %CV
i-STAT	1	0.58	5.2	2.3	3.1	6.1
	2	2.36	4.2	2.4	4.0	5.9
	3	33.65	5.0	3.3	2.6	6.1
Site 1	1	0.49	6.3	2.9	7.0	9.4
	2	2.01	5.3	4.1	9.7	11.4
	3	31.52	6.5	2.9	5.3	8.4

Site	Control Level	Mean	Within-Lot %CV	Lot-to-Lot %CV	Vial-to-Vial %CV	Total %CV
Site 2	1	0.54	4.7	4.0	6.2	8.2
	2	2.23	5.3	3.0	6.2	8.3
	3	32.90	5.4	3.1	5.5	7.9
Site 3	1	0.50	5.3	5.7	2.4	7.3
	2	2.04	5.0	6.6	4.2	8.3
	3	29.20	6.4	2.9	4.5	7.8

b. Linearity/assay reportable range:

Whole blood and plasma samples from three donors were tested. For whole blood the original cTnI negative samples were spiked and assayed in duplicate in three separate i-STAT cTnI cartridges. The samples were diluted in equal masses with the original negative samples and assayed under the same conditions. For plasma the three samples were tested as original samples and combined in equal masses.

Recovery Study Whole Blood

Whole Blood Sample	Concentration	Diluted Concentration	% Recovery
A	2.05	1.04	101
B	6.31	3.14	100
C	27.04	14.05	104

Recovery Study Plasma

Plasma Sample	Concentration	Diluted Concentration	% Recovery
A	2.41	-	-
B	7.50	-	-
C	29.35	-	-
A+B	-	4.69	95
B+C	-	18.90	103
A+C	-	16.89	106

Performance characteristics of i-STAT cTnI have been established in the range from 0.02 to 35.00 ng/mL.

c. *Traceability (controls, calibrators, or method):*
Not applicable

d. *Detection limit:*
Analytical sensitivity was determined to be 0.02 ng/mL based on two standard deviations from a sample with zero concentration.

The 20% and 10% functional sensitivities were estimated from whole blood samples measurements to be 0.07 and 0.1 ng/mL, respectively.

e. *Analytical specificity:*
Related muscle proteins were tested for cross reactivity at concentrations of 1000 ng/mL.

Cross reactants	% Crossreactivity
Troponin C (cardiac)	<0.002
Troponin T (cardiac)	0.65
Troponin I (skeletal)	<0.002
Troponin T (skeletal)	<0.002

Interference testing was performed with the substances listed below and found to have less than a 10% change at the concentrations listed below, when added to a plasma pool containing approximately 2 ng/mL of cTnI.

Generic Name	Test Level uMol/L	Average cTnI ng/mL	% change
Control	NA	1.75	NA
Acetaminophen	1660	1.76	0.6
Acetylsalicylic Acid	3330	1.78	1.7
Allopurinol	294	1.84	5.1
Ampicillin	349	1.78	1.7
Ascorbic Acid	227	1.78	1.7
Atenolol	37.6	1.8	2.9
Caffeine	308	1.83	4.6
Captopril	23	1.83	4.6
Chloramphenicol	155	1.79	2.3
Diclofenac	169	1.75	0
Digoxin	6.15	1.81	3.4
Dopamine	5.87	1.67	-4.6
Enalaprilat	0.86	1.81	3.4

Generic Name	Test Level uMol/L	Average cTnI ng/mL	% change
Erythromycin	81.6	1.74	-0.6
Furosemide	181	1.82	4.0
Sodium Heparin	36 U/mL	1.58	-9.7
Sodium Heparin	90 U/mL	1.41	-19.4
Ibuprophen	2425	1.79	2.3
Isorbide Dinitrate	636	1.72	-1.7
Methyldopa	71	1.85	5.7
Nicotine	6.2	1.76	0.6
Nifedipine	1.156	1.79	2.3
Phenytoin	198	1.76	0.6
Propranolol	7.71	1.82	4.0
Salicylic Acid	4340	1.69	-3.4
Theophylline	222	1.77	1.1
Verapamil	4.4	1.82	4.0
Warfarin	64.9	1.79	2.3

f. Assay cut-off:
The reference range was established from 162 whole blood and plasma samples of apparently healthy donors using duplicate measures with three different lots of i-STAT cTnI cartridges. The 0 to 97.5% range results spanned from 0 to 0.03 ng/mL.

2. Comparison studies:

a. Method comparison with predicate device:
Studies were carried out at three clinical sites with patients in any hospital department who presented with acute, severe, and prolonged chest pain. Up to three samples, drawn at different times, could be taken from any one patient. Data from 189 samples were included in the data set. All testing was performed by end-user personnel. Samples were drawn by venipuncture using heparinized evacuated tubes. Operators analyzed whole blood in duplicate using three different i-STAT cTnI cartridges, for a total of 6 whole blood measurements. The tubes were then centrifuged and analyzed by the laboratory in duplicate using the predicate device and again in duplicate for three different i-STAT cTnI cartridges, for a total of 6 plasma measurements. Analysis of the method comparison data was undertaken in accordance with the recommendations set forth in the NCCLS guideline EP9-A2: *Method Comparison and Bias Estimation Using Patient Samples*. Of 2241 test method data points, 3 were determined to be within-method outliers and excluded from subsequent analysis. Deming regression analyses were performed on the first replicate of each sample, on average duplicate values and on the whole data set against the predicate. Results from a

representative subset with n=189 and a range from 0 to 46.27 ng/mL gave a slope of 0.883, an intercept of 0.029, and a correlation (r) of 0.975.

b. Matrix comparison:
Deming regression analysis was performed comparing the plasma data set against the whole blood data set. A slope of 1.002, an intercept of -0.01, and a correlation (r) of 0.991 were obtained.

3. Clinical studies:
   a. Clinical sensitivity:
   Not performed

   b. Clinical specificity:
   Not performed

   c. Other clinical supportive data (when a and b are not applicable):

4. Clinical cut-off:
   Clinical cut-off was not independently established for this device.

5. Expected values/Reference range:
   The reference range was established from 162 whole blood and plasma samples of apparently healthy donors using duplicate measures with three different lots of i-STAT cTnI cartridges. The 0 to 97.5% range results spanned 0 to 0.03 ng/mL

M. Instrument Name:
i-STAT 1 Analyzer

N. System Descriptions:
1. Modes of Operation:
   The i-STAT 1 Analyzers are portable clinical analyzers designed to be used at the point of patient care. The analyzers employ single-use cartridges containing biosensor chips to perform diagnostic tests on whole blood. Whole blood is introduced into the sample well of the cartridge at the blood entry port. After closure, the cartridge is inserted into the cartridge door of the analyzer. Insertion of the cartridge initiates a precisely controlled and monitored sequence of steps performed by the instrument without user intervention. Results are calculated, displayed and stored in memory to be transmitted at some later time via an infra red link for printing and database storage.

2. Software:
   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:
   Yes ____X____ or No _____

3. Sample Identification:
   Bar code reader is incorporated into the system.

4. Specimen Sampling and Handling:
   Whole blood samples are applied directly into the sample well of the cartridge.

5. Assay Types:
   The i-STAT analyzer is cable of performing assays for sodium, potassium, chloride, ionized calcium, glucose, blood urea nitrogen, pH, carbon dioxide, oxygen, hematocrit, creatinine, lactate, Celite Activated Clotting Time (ACT), and Prothrombin Time (PT).

6. Reaction Types:
   All assays are performed in self-contained cartridges which output an amperometric signal which is detected and processed by the analyzer.

7. Calibration:
   All cartridges contain an enclosed aqueous calibrator (with the exception of ACT and PT).

8. Quality Control:
   A set of controls, the i-STAT Cardiac Markers Control set is available.

O. Other Supportive Instrument Performance Characteristics Data Not Covered In The "L. Performance Characteristics" Section Of the SE Determination Decision Summary.

Not Applicable

P. Conclusion:

Based upon the information provided, I recommend that the i-STAT cTnI Test be found substantially equivalent to predicate devices according to 21 CFR §862.1215.